REMARKS

The Office Action mailed October 04, 2004, has been carefully reviewed.

Claims 12 – 15 and 17-23 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Application Publication 2004/0091500 A1, (herein after referred to as the "alleged prior art").

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Reconsideration and allowance of the present application are respectfully requested in view of the foregoing amendments and the following additional remarks which have addressed all the grounds for objection or rejection or otherwise have rendered them moot.

Claim Rejections under 35 U.S.C. § 102(e)

Claims 12 – 15 and 17-23 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Application Publication 2004/0091500 A1, (herein after referred to as the "alleged prior art"). The Examiner contends that the alleged prior art teaches a method of treating or preventing an allergic disorder by administering a derivative of an allergenic protein having reduced allergenic activity, wherein said protein is administered with adjuvant, every two weeks and within the range of 1-50 times and at concentrations of 0.0001 to 1000 micrograms, wherein said protein administered is either Bet v1 or Vespula. Applicants respectfully disagree with the Examiner's assertions and traverse as follows.

There is a fundamental difference between the methodology taught by the alleged prior art and the methodology of the instant invention. That fundamental difference is embodied in previously presented, now canceled, claim 13 referring to the concept of "blocking antibodies" and applicants respectfully observe that that fundamental difference may have escaped the

Examiner's perception, leading to the erroneous conclusion that previously presented, and now canceled claim 13, was anticipated by the alleged prior art. The Supplemental Information Disclosure Statement filed herewith, discloses a review article entitled, "Renaissance of the Blocking Antibody Concept in Type I Allergy" co-authored by Flicker and Valenta for the Examiner's convenience.

As the Examiner is aware, formation of IgE antibodies against per se harmless antigens (i.e. allergens) is the hallmark and key pathomechanism of type I allergy, a hypersensitivity disease affecting more than 25% of the population. The methodology of the present invention is based on the theory that allergen-specific IgG antibodies, termed blocking antibodies, can antagonize the cascade of allergic inflammation resulting from allergen recognition by IgE antibodies. The instant invention is based on the rationale that blocking antibodies inhibit allergen-induced release of inflammatory mediators from basophils and mast cells as well as IgE-facilitated allergen presentation to T cells, thus leading to suppression of T cell activation. Furthermore, the development of blocking antibodies is associated with reduced boosts of allergen-specific IgE production in patients receiving allergen-specific immunotherapy of the present invention. Thus blocking antibodies have protective activity by inhibiting immediate as well as late inflammatory responses and long-term ameliorating activity on the allergic immune response by antagonizing the underlying IgE production. Induction of blocking antibodies is thus an important mechanism underlying allergen-specific immunotherapy. See Specification pages 5 and 6.

New claims 24 to 48 embody that fundamental component of previously presented, now canceled claim 13, and particularly assert and distinctly claim **derivatives** (not necessarily allergenic) capable of, **in vivo**, inducing IgG antibody production, while simultaneously inhibiting the binding of and or decreasing the production of allergen-specific IgE against naturally occurring allergens , as the allergenic derivatives of the present invention.

Contrastingly, the alleged prior art teaches **allergenic derivatives** characterized by reduced binding of IgE compared to the naturally occurring allergen as the recombinant allergens of the prior art. Specifically, paragraph 0030 of the alleged prior art teaches reduced binding of IgE by substitution of surface exposed amino acids while conserving α-carbon backbone tertiary structure. The methodology of the alleged prior art goes through an elaborate scheme of structural characterization of naturally occurring allergens followed by targeted amino acid substitution at B-cell eptitopic site such that the said tertiary backbone of the naturally occurring allergen is essentially preserved. Particularly, the structural elucidation of naturally occurring allergens is followed by targeted substitution at putative IgE binding sites such that the tertiary structure of the allergen is preserved.

The methodology of the instant invention does not concern itself with structural conservation of the allergenic derivative, but instead chooses such derivatives, of whatever structural configuration, derived by substitution, fragmentation or any other means in the art, and is capable of inducing sufficient IgG production in vivo, such that the binding of allergen-specific IgE to the naturally occurring allergen is substantially reduced, if not totally eliminated, and/or simultaneously inhibits the production of allergen-specific IgE.

Thus, while the alleged prior art involves the concept of dominant IgE binding epitopes and the therapeutic concept of initiating a new protective immune response (see paragraph 0030), the instant invention is concerned with the induction of IgG as "protective antibodies", ie antibodies which possibly prevent IgE from binding to the respective wild type protein from which the derivative is derived. See page 4.

Thus, roughly speaking, while the alleged prior art targets the epitopic specificity of IgE, the instant invention is concerned with the epitopic specificity of IgG, and the Applicants believe, teaches a far less experimentally intensive technology based on in vivo animal models.

It must be asserted for clarity, that the Applicants of the present invention are not arguing that the structurally conserved allergenic derivatives of the alleged prior art are

incapable of inducing IgG production. Paragraph 0046 mentions that the theory of the alleged prior art (initiation of a new Th1-type immune response involving tertiary epitope recognition by B-cells) is supported by observations that levels of specific IgE are unaffected by successful vaccination treatment, and that successful treatment is **often** accompanied by a substantial rise in allergen specific IgG4. The fundamental point of departure however, is that the instant invention teaches a method of treating and or preventing allergic disorders using derivatives of naturally occurring allergens such that in vivo administration of the derivative is **always** accompanied by substantial rise in IgG wherein allergen specific IgE binding to the derivative is substantially reduced or eliminated.

Further, unlike the alleged prior art, the instant invention teaches and claims a precise scheme of vaccination consistent with the immunotherapeutic regimen that accounts for optimal elicitation of blocking antibody production. See Page 4, paragraph 7. For at least the fundamental difference in methodology, Applicants assert that the alleged prior art does not disclose identically what is claimed in the instant invention and the basis of the prior rejection has been effectively rendered moot by the "blocking" antibody language of the new claims. Applicants respectfully ask that this ground for rejection be withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicants submit that there is no basis for applying the previous rejection to the pending claims and withdrawal of the rejections is respectfully requested. The claims are believed to be in condition for allowance, and Applicant earnestly solicits from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, she is invited to contact the undersigned at his earliest convenience.

Respectfully submitted,

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